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**Term:** 118 same bone marrow

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| USPT,PGPB,JPAB,EPAB | isolated or cultured | 326826 | L2 |
| USPT,PGPB,JPAB,EPAB | stroma or mesenschymal | 2420 | L1 |

L8: Entry 3 of 34 File: USPT Oct 31, 2000

US-PAT-NO: 6140039
DOCUMENT-IDENTIFIER: US 6140039 A
TITLE: Three-dimensional filamentous tissue having tendon or ligament function
DATE-ISSUED: October 31, 2000

US-CL-CURRENT: 435/1.1; 424/423, 424/93.7, 435/177, 435/178, 435/179, 435/180, 435/395, 435/398, 435/399, 435/402

APPL-NO: 9/ 237980
DATE FILED: January 25, 1999

PARENT-CASE:
This is a continuation application of U.S. patent application Ser. No. 08/487,749, filed Jun. 7, 1995 (U.S. Pat. No. 5,863,531); which is a continuation-in-part of U.S. patent application Ser. No. 08/254,096, filed Jun. 6, 1994 (abandoned); which is a continuation-in-part of U.S. patent application Ser. No. 08/131,361 filed Oct. 4, 1993 (U.S. Pat. No. 5,443,950); which is a divisional of U.S. patent application Ser. No. 07/575,518 filed Aug. 30, 1990 (U.S. Pat. No. 5,266,480); which is a divisional of U.S. patent application Ser. No. 07/402,104 filed Sep. 1, 1989 (U.S. Pat. No. 5,032,508); which is a continuation-in-part of application Ser. No. 07/242,096, filed Sep. 8, 1988 (U.S. Pat. No. 4,963,489; which is a continuation-in-part of U.S. patent application Ser. No. 07/038,110 filed Apr. 14, 1987 (abandoned); which is a continuation-in-part of U.S. patent application Ser. No. 07/036,154 filed Apr. 3, 1987 (U.S. Pat. No. 4,721,096); which is a continuation of application Ser. No. 06/853,569 filed Apr. 18, 1986 (abandoned), each of which is incorporated herein in its entirety.

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L8: Entry 14 of 34 File: USPT Jul 28, 1998

US-PAT-NO: 5785964
DOCUMENT-IDENTIFIER: US 5785964 A
TITLE: Three-dimensional genetically engineered cell and tissue culture system
DATE-ISSUED: July 28, 1998

US-CL-CURRENT: 424/93.21; 424/93.1, 424/93.2, 424/93.3, 435/320.1, 435/325, 800/14

APPL-NO: 8/ 418238
DATE FILED: April 6, 1995

PARENT-CASE:
The present application is a division of application Ser. No. 08/131,361, filed Oct. 4, 1993, now U.S. Pat. No. 5,443,950; which is a division of Ser. No. 07/575,518, filed Aug. 30, 1990, U.S. Pat. No. 5,266,480; which is a division of Ser. No. 07/402,104, filed Sep. 1, 1989, U.S. Pat. No. 5,032,508; which is a continuation-in-part of Ser. No. 07/242,096, filed Sep. 8, 1988, U.S. Pat. No. 4,963,489; which is a continuation-in-part of Ser. No. 07/038,110, filed Apr. 14, 1987, abandoned; which is a continuation-in-part of 07/036,154, filed Apr. 3, 1987, U.S. Pat. No. 4,721,096 which is a continuation of Ser. No. 06/853,569, filed Apr. 18, 1986, abandoned; each of which is incorporated by reference herein in its entirety.

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L8: Entry 20 of 34 File: USPT Jul 30, 1996

US-PAT-NO: 5541107
DOCUMENT-IDENTIFIER: US 5541107 A
TITLE: Three-dimensional bone marrow cell and tissue culture system
DATE-ISSUED: July 30, 1996

US-CL-CURRENT: 435/29; 424/422, 424/484, 424/572, 435/1.1, 435/284.1, 435/289.1, 435/32, 435/347

APPL-NO: 8/ 418234
DATE FILED: April 6, 1995

PARENT-CASE:
This is a division, of application Ser. No. 08/131,361, filed Oct. 4, 1993, U.S. Pat. No. 5,443,950, which is a division of Ser. No. 07/575,518, filed Aug. 30. 1990, U.S. Pat. No. 5,266,480; which is a division of Ser. No. 07/402,104, filed Sep. 1, 1989. U.S. Pat. No. 5,032,508; which is a continuation-in-part of Ser. No. 07/242,096, filed Sep. 8, 1988, U.S. Pat. No. 4,963,489; which is a continuation-in-part of Ser. No. 07/038,110, filed April 14, 1987, abandoned; which is a continuation-in-part of 07/036,154, filed Apr. 3, 1987, U.S. Pat. No. 4,721,096 which is a continuation of Ser. No. 06/853,569, filed Apr. 18. 1986, abandoned; each of which is incorporated by reference herein in its entirety.

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L16: Entry 31 of 60 File: USPT Aug 24, 1999

US-PAT-NO: 5942496
DOCUMENT-IDENTIFIER: US 5942496 A
TITLE: Methods and compositions for multiple gene transfer into bone cells
DATE-ISSUED: August 24, 1999

US-CL-CURRENT: 514/44; 424/93.21, 435/320.1, 435/325, 435/455, 435/458, 435/69.1

APPL-NO: 8/ 316650
DATE FILED: September 30, 1994

PARENT-CASE:
The present application is a continuation-in-part of U. S. Ser. No. 08/199,780, now U.S. Pat. No. 5,763,416, filed Feb. 18, 1994; the entire text and figures of which disclosure are specifically incorporated herein by reference without disclaimer. The United States government has certain rights in the present invention pursuant to Grants AR40673, AR40679 and AR4242 from the National Institutes of Health.

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L16: Entry 32 of 60 File: USPT Aug 10, 1999

US-PAT-NO: 5935849
DOCUMENT-IDENTIFIER: US 5935849 A
TITLE: Methods and compositions of growth control for cells encapsulated within bioartificial organs
DATE-ISSUED: August 10, 1999

US-CL-CURRENT: 435/325; 435/375, 435/377, 435/400

APPL-NO: 8/ 279773
DATE FILED: July 20, 1994

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L16: Entry 36 of 60 File: USPT Jan 12, 1999

US-PAT-NO: 5858747
DOCUMENT-IDENTIFIER: US 5858747 A

TITLE: Control of cell growth in a bioartificial organ with extracellular matrix coated microcarriers

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schinstine; Malcolm | Ben Salem | PA | N/A | N/A |
| Shoichet; Molly S. | Toronto | N/A | N/A | CAX |
| Gentile; Frank T. | Warwick | RI | N/A | N/A |
| Hammang; Joseph P. | Barrington | RI | N/A | N/A |
| Holland; Laura M. | Horsham | PA | N/A | N/A |
| Cain; Brian M. | Everett | MA | N/A | N/A |
| Doherty; Edward J. | Mansfield | MA | N/A | N/A |
| Winn; Shelley R. | Smithfield | RI | N/A | N/A |
| Aebischer; Patrick | Lutry | N/A | N/A | CHX |

US-CL-CURRENT: 435/182; 424/422, 424/93.21, 424/93.7, 435/176, 435/177, 435/178, 435/289.1, 435/377, 435/382, 435/395, 435/403

CLAIMS:

We claim:
1. A method for controlling distribution of a core of living cells encapsulated by a biocompatible jacket in a bioartificial organ comprising growing the cells on microcarriers prior to encapsulation to produce microcarriers containing cells then loading the microcarriers containing cells in the bioartificial organ.
2. The method of claim 1 wherein the microcarriers are selected from the group consisting of dextran microcarriers, gelatin microcarriers and glass microcarriers.
3. The method of claim 1 wherein the cells are selected from the group consisting of primary cells and immortalized cell lines.
4. The method of claim 1 wherein the cells are modified to secrete a biologically active molecule.
5. The method according to claim 4 wherein the cells secrete a biologically active molecule from the group consisting of hormones, cytokines, growth factors, trophic factors, angiogenesis factors, antibodies, blood coagulation factors, lymphokines and enzymes.
6. The method according to claim 1 wherein the microcarriers containing cells are suspended in a proliferation inhibiting hydrogel matrix prior to encapsulation in the bioartificial organ.
7. A bioartificial organ comprising:
(a) a biocompatible jacket; and
(b) a core comprising of living cells grown on microcarriers prior to encapsulation to produce microcarriers containing cells said microcarriers containing cells then loaded into and encapsulated by the biocompatible jacket in the bioartificial organ.
8. The bioartificial organ of claim 7 wherein the microcarrier is selected from the group consisting of dextran microcarriers, gelatin microcarriers and glass microcarriers.
9. The bioartificial organ of claim 7 wherein the jacket comprises a material

9. The bioartificial organ of claim 7 wherein the jacket comprises a material selected from the group consisting of polyacrylates, polyvinylidenes, polyvinyl chloride copolymers, polyurethanes, polystyrenes, polyamides, cellulose acetates, cellulose nitrates, polysulfones, polyphosphazenes, polyacrylonitriles, poly(acrylonitrile/covinyl chloride), copolymers thereof and mixtures thereof.
10. The bioartificial organ of claim 7 wherein the cells are selected from the group consisting of primary cells and immortalized cell lines.
11. The bioartificial organ of claim 7 wherein the microcarriers containing cells are suspended in a proliferation inhibiting hydrogel matrix prior to encapsulation in the bioartificial organ.

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L16: Entry 37 of 60 File: USPT Jan 5, 1999

US-PAT-NO: 5855610
DOCUMENT-IDENTIFIER: US 5855610 A

TITLE: Engineering of strong, pliable tissues

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Vacanti; Joseph P. | Winchester | MA | N/A | N/A |
| Breuer; Christopher K. | Brighton | MA | N/A | N/A |
| Chaignaud; Beverly E. | Brookline | MA | N/A | N/A |
| Shin'oka; Toshiraru | Brookline | MA | N/A | N/A |

US-CL-CURRENT: 623/2.13

CLAIMS:

We claim:
1. A cell-matrix structure comprising
a fibrous matrix formed of a biocompatible, biodegradable synthetic polymer, and seeded with dissociated human cells,
wherein the matrix is configured to form a tissue structure having mechanical strength and flexibility or pliability,
wherein the cell-matrix structure is formed by seeding the matrix, implanting the seeded matrix into a recipient human or animal for a period of time sufficient to form extracellular matrix; and harvesting of the resulting cell-matrix structure.
2. The cell-matrix structure of claim 1 wherein the matrix is configured to form a tube.
3. The cell-matrix structure of claim 1 wherein the matrix is configured to form a valve in a blood vessel, intestine, or heart.
4. The cell-matrix structure of claim 3 wherein the matrix is configured to form a heart valve.
5. The cell-matrix structure of claim 1 wherein the cells are selected from the group of consisting of parenchymal and connective tissue cells.
6. A tissue-engineered heart valve formed of a porous polymeric matrix seeded with dissociated endothelial and fibroblast cells, wherein the cells form extracellular matrix following implantation into a human or animal recipient, and wherein the extracellular matrix is shaped to form a heart valve.
7. The heart valve of claim 6 wherein the matrix is formed of a polymer selected from the group consisting of poly(lactic acid), poly(glycolic acid), and combinations thereof.
8. The heart valve of claim 7 wherein the matrix is formed of polymer fibers having an interstitial spacing of between 100 and 300 microns and having pore sizes and structure to control the pattern and extent of fibroblastic tissue ingrowth following implantation.
9. The heart valve of claim 7 wherein the matrix was seeded with dissociated cells selected from the group consisting of fibroblasts, myofibroblasts, and endothelial cells and includes elastin fibers.

L19: Entry 8 of 63 File: USPT Jul 11, 2000

DOCUMENT-IDENTIFIER: US 6087113 A
TITLE: Monoclonal antibodies for human mesenchymal stem cells

DEPR:
The osteo-chondrogenic potential of cultured marrow-derived mesenchymal stem cells was also assayed by loading cells in diffusion chambers and surgically implanting them intraperitoneally into nude mice. The cells were obtained from the same cultures used in the ceramic assays (Table 2), and the diffusion chambers were implanted into the peritonea of the same nude mice which received subcutaneous ceramic-marrow-derived mesenchymal stem cell grafts. After incubations for 3-10 weeks, the chambers were harvested and the presence of bone and cartilage formation determined by histological evaluation. In contrast to the presence of bone in grafts of ceramic and cultured cells from cancellous bone, no bone or cartilage was observed in any of the diffusion chambers containing cultured cancellous bone marrow-derived mesenchymal stem cells even after 10 weeks incubation (Table 2). Cultured iliac aspirate marrow-derived mesenchymal stem cells also failed to produce bone or cartilage in the diffusion chambers. Instead, hypocellular sparse fibrous tissue was observed in most of the chambers.

DEPR:
The absence of bone formation in diffusion chambers suggests that the ceramic assay may be a more sensitive assay for differentiation of bone from marrow cells. Bab, et al. (Bab, I., Passi-Even, L., Gazit, D., Sekeles, E., Ashton, B. A., Peylan-Ramu, N., Ziv, I., and Ulmansky, M.; Osteogenesis in in vivo diffusion chamber cultures of human marrow cells, Bone and Mineral, 4:373, 1988) observed bone in four of eight diffusion chambers implanted with human marrow from two child donors; however, these authors failed to observe bone when whole marrow from older donors was incubated in diffusion chambers in nude mice. In addition, Davies (Davies, J. E., Human bone marrow cells synthesize collagen, in diffusion chambers, implanted into the normal rat, Cell. Biol. Int. Rep. 11(2):125, 1987) did not observe bone formation in diffusion chambers inoculated with fresh marrow from a five year old female, nor was bone formation observed by Ashton, et al. (Ashton, B. A., Cave, F. A., Williamson, M., Sykes, B. C., Couch, M., and Poser, J. W.; Characterization of cells with high alkaline phosphatase activity derived from human bone and marrow, preliminary assessment of their osteogenicity, Bone, 5:313-319, 1985) in diffusion chambers inoculated with cultured fibroblasts from composite pieces of bone and marrow from children and young adults.

DEPR:
Cultured marrow-derived mesenchymal stem cells originating from femoral head cancellous bone appear to be more osteogenic than cultured marrow-derived mesenchymal stem cells from iliac aspirated marrow, 9 out of 9 cancellous bone marrow samples produced bone in ceramics, whereas, 3 out of 4 aspirated marrow-derived mesenchymal stem cell samples produced bone in ceramics. In addition, bone was present in fewer pores in ceramics grafted with aspirated marrow-derived mesenichymal stem cells than ceramics grafted with femoral head marrow-derived mesenchymal stem cells. The reasons for the differences may be associated with the proximity of the harvested marrow stromal cells to the bone surface in the original tissue. Ashton, et al. (Ashton, B. A., Eaglesom, C. C., Bab, I., and Owen, M. E., Distribution of fibroblastic colony-forming cells in rabbit bone marrow and assay of their osteogenic potential by an in vivo diffusion chamber method, Calcif. Tissue Int., 36:83, 1984) showed that cultured rabbit marrow stromal cells differ in their colony forming potential in vitro and osteogenic potential in diffusion chambers depending on their original proximity to the endosteal surface. Cells closest to the endosteal surface were shown to

have four times the colony forming efficiency as compared to cells of the core. In the present study, marrow from cancellous bone was harvested by vigorous vortexing to separate the cancellous bone from the marrow cells. This likely produces a population of marrow enriched in cells derived from near the endosteal surface, as compared to aspirate marrow where vigorous separation of marrow cells from cancellous bone is not possible. The inventors observed a consistently higher initial number of adherent cells from cancellous bone marrow as compared to aspirate marrow, which is similar to the observations of Ashton, et al. (Ashton, B. A., Eaglesom, C. C., Bab, I., and Owen, M. E., Distribution of fibroblastic colony-forming cells in rabbit bone marrow and assay of their osteogenic potential by an in vivo diffusion chamber method, Calcif. Tissue Int., 36:83, 1984).

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L16: Entry 43 of 60 File: USPT Dec 1, 1998

US-PAT-NO: 5843431
DOCUMENT-IDENTIFIER: US 5843431 A

TITLE: Controlling proliferation of cells before and after encapsulation in a bioartificial organ by gene transformation

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Schinstine; Malcolm | Ben Salem | PA | N/A | N/A |
| Shoichet; Molly S. | Toronto | N/A | N/A | CAX |
| Gentile; Frank T. | Warwick | RI | N/A | N/A |
| Hammang; Joseph P. | Barrington | RI | N/A | N/A |
| Holland; Laura M. | Horsham | PA | N/A | N/A |
| Cain; Brian M. | Everett | MA | N/A | N/A |
| Doherty; Edward J. | Mansfield | MA | N/A | N/A |
| Winn; Shelley R. | Smithfield | RI | N/A | N/A |
| Aebischer; Patrick | Lutry | N/A | N/A | CHX |

US-CL-CURRENT: 424/93.21; 424/422, 424/93.7, 435/174, 435/178, 435/377, 435/382, 435/395, 435/467

CLAIMS:

We claim:
1. A method for controlling distribution of cells within an implantable bioartificial organ comprising the steps of:
(a) transforming the cells with a proliferation-promoting gene operatively linked to a regulatable promoter wherein the regulatable promoter is activated in vitro to achieve expression of the proliferation-promoting gene, resulting in proliferation of the transformed cells in vitro; and
(b) inserting the cells from (a) in a bioartificial organ and inactivating the regulatable promoter either before or after inserting the cells in the bioartificial organ such that expression of the proliferation-promoting gene is inhibited to reduce or stop proliferation of the cells in the bioartificial organ in vivo in a host.
2. The method according to claim 1, wherein the proliferation promoting gene is an oncogene.
3. The method according to claim 2, wherein the oncogene is selected from the group consisting of c-myc, v-mos, v-Ha-ras, SV40 early region and E1-A.
4. The method according to claim 1, wherein the regulatable promoter is selected from the group consisting of tetracycline-responsive promoters, interferon-responsive promoters, glucocorticoid-responsive promoters and retroviral long terminal repeat promoters.
5. The method according to claim 4, wherein the interferon-responsive promoter is the Mx1 promoter and the proliferation-promoting gene is SV40 early region.
6. The method of claim 1 further comprising the step of:
(c) reactivating the regulatable promoter in vivo in the bioartificial organ such that expression of the proliferation-promoting gene is achieved, resulting in further proliferation of the cells in the bioartificial organ.
7. A method for controlling distribution of cells within an implantable bioartificial organ comprising the steps of:

(a) transforming the cells with a proliferation-suppressing gene operatively linked to a regulatable promoter wherein the regulatable promoter is inactivated in vitro to inhibit expression of the proliferation-suppressing gene, resulting in proliferation of the transformed cells in vitro; and
(b) inserting the cells from (a) in a bioartificial organ and activating the regulatable promoter either before or after inserting the cells in the bioartificial organ such that expression of the proliferation-suppressing gene occurs to reduce or stop proliferation of the cells in the bioartificial organ in vivo in a host.

8. The method according to claim 7, wherein the proliferation-suppressing gene is a tumor suppressor gene selected from the group consisting of the p53 gene and the RB gene.

9. A method for controlling distribution of cells within an implantable bioartificial organ comprising the steps of:
(a) transforming the cells with a differentiation-inducing gene operatively linked to a regulatable promoter wherein the regulatable promoter is inactivated in vitro to inhibit expression of the differentiation-inducing gene, resulting in proliferation of the transformed cells invtro; and
(b) inserting the cells from (a) in a bioartificial organ and activating the regulatable promoter either before or after inserting the cells in the bioartificial organ such that expression of the differentiation-inducing gene occurs to reduce or stop proliferation of the cells in the bioartificial organ in vivo in a host.

10. The method according to claim 9, wherein the differentiation-inducing gene is the high mobility group chromosomal protein 14.

L19: Entry 45 of 63 File: USPT Mar 30, 1993

US-PAT-NO: 5197985
DOCUMENT-IDENTIFIER: US 5197985 A

TITLE: Method for enhancing the implantation and differentiation of marrow-derived mesenchymal cells

DATE-ISSUED: March 30, 1993

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Caplan; Arnold I. | Cleveland Heights | OH | 44121 | N/A |
| Haynesworth; Stephen E. | Cleveland Heights | OH | 44118 | N/A |

US-CL-CURRENT: 128/898; 530/838, 530/840, 623/923

CLAIMS:

Having thus described the preferred embodiment, the invention is now claimed to be:
1. A method for inducing human marrow-derived mesenchymal stem cells to differentiate into bone-forming cells, comprising:
a) providing human marrow-derived mesenchymal stem cells that have been isolated, purified and culturally expanded from a bone marrow specimen by adding the bone marrow specimen to a medium which contains factors which stimulate mesenchymal cell growth without differentiation and allows, when cultured, for selective adherence of only the mesenchymal stem cells to a substrate surface;
b) applying the isolated, purified and culturally expanded human marrow-derived mesenchymal stem cells to a porous carrier; and,
c) implanting the porous carrier containing the culturally expanded human marrow-derived mesenchymal stem cells into an environment containing factors necessary for differentiating the human mesenchymal stem cells into bone cells.
2. The method of claim 1, wherein said environment is in vivo.
3. The method of claim 1, wherein said porous carrier comprises about 60% hydroxyapatite and about 40% tricalcium phosphate.
4. A method for repairing skeletal defects comprising:
a) providing marrow-derived human mesenchymal stem cells that have been culturally expanded from isolated and purified human marrow-derived mesenchymal stem cells which have been isolated from a bone marrow specimen by adding the bone marrow specimen to a medium which contains factors which stimulate mesenchymal cell growth without differentiation and allows, when cultured, for selective adherence of only the mesenchymal stem cells to a substrate surface;
b) applying the culturally expanded marrow-derived human mesenchymal stem cells to a porous carrier; and,
c) implanting the porous carrier containing the culturally expanded purified human marrow-derived mesenchymal stem cells into the defective skeletal tissue.
5. The method of claim 4, wherein said porous carrier is comprised of about 60% hydroxyapatite and about 40% tricalcium phosphate.
6. A method for repairing skeletal defects comprising:
a) providing a bone marrow specimen containing human marrow-derived mesenchymal stem cells and bone pieces;
b) adding the bone marrow specimen to a medium thereby producing a bone marrow specimen-medium mixture, wherein said medium contains factors which stimulate human marrow-derived mesenchymal stem cell growth without differentiation and allows, when cultured, for selective adherence of only the human marrow-derived mesenchymal stem cells to a substrate surface;

c) separating the bone pieces from the bone marrow medium mixture;
d) dissociating marrow cells in the bone marrow specimen-medium mixture into single cells;
e) culturing the dissociated marrow cells in the bone marrow specimen-medium mixture thereby selectively adhering only the human mesenchymal stem cells to the substrate surface;
f) separating non-adherent matter from the substrate surface, thereby producing isolated culturally expanded human mesenchymal stem cells;
g) removing remaining adherent isolated and culturally expanded human mesenchymal stem cells from the substrate surface with a releasing agent;
h) applying the isolated and culturally expanded human marrow-derived mesenchymal stem cells to a porous carrier comprised of about 60% hydroxyapatite and about 40% tricalcium phosphate; and,
i) implanting the porous carrier containing the culturally expanded human marrow-derived mesenchymal stem cells into the defective skeletal tissue.
7. The method of claim 6, wherein said porous carrier is comprised of about 60% hydroxyapatite and about 40% tricalcium phosphate.
8. The method of claim 6, wherein said medium is comprised of BGJ.sub.b Medium with 10% fetal bovine serum.
9. The method of claim 6, wherein said medium is comprised of F-12 Nutrient Mixture.
10. A method for inducing marrow-derived human mesenchymal stem cells to differentiate into cartilage-forming cells, comprising:
a) providing human marrow-derived mesenchymal stem cells that have been culturally expanded from isolated and purified human marrow-derived mesenchymal stem cells which have been isolated from a bone marrow specimen by adding the bone marrow specimen to a medium which contains factors which stimulate mesenchymal cell growth without differentiation and allows, when cultured, for selective adherence of only the mesenchymal stem cells to a substrate surface;
b) applying the culturally expanded human marrow-derived mesenchymal stem cells to a carrier formatted to promote round cell morphology;
c) implanting the carrier containing the culturally expanded human marrow-derived mesenchymal stem cells into an environment containing factors necessary for differentiating the human mesenchymal stem cells into cartilage-forming cells.
11. A method for repairing damaged articular cartilage comprising:
a) providing human marrow-derived mesenchymal stem cells that have been culturally expanded from isolated and purified human marrow-derived mesenchymal stem cells which have been isolated from a bone marrow specimen by adding the bone marrow specimen to a medium which contains factors which stimulate mesenchymal cell growth without differentiation and allows, when cultured, for selective adherence of only the mesenchymal stem cells to a substrate surface;
b) applying the culturally expanded human marrow-derived mesenchymal stem cells to a carrier formatted to promote round cell morphology; and,
c) implanting the carrier containing the culturally expanded human marrow-derived mesenchymal stem cells into the damaged articular cartilage.
12. A method for repairing damaged articular cartilage comprising:
a) providing a bone marrow specimen containing human mesenchymal stem cells and bone pieces;
b) adding the bone marrow specimen to a medium thereby producing a bone marrow specimen-medium mixture, wherein said medium contains factors which stimulate human marrow-derived mesenchymal stem cell growth without differentiation and allows, when cultured, for selective adherence of only the human marrow-derived mesenchymal stem cells to a substrate surface;
c) separating the bone pieces from the bone marrow specimen-medium mixture;
d) dissociating marrow cells in the bone marrow specimen-medium mixture into single cells;
e) culturing the dissociated marrow cells in the bone marrow medium specimen-mixture thereby selectively adhering only the human mesenchymal stem cells to the substrate surface;
f) separating non-adherent matter from the substrate surface, thereby producing isolated culturally expanded human marrow-derived mesenchymal stem cells;
g) removing remaining adherent isolated culturally expanded human mesenchymal stem cells from the substrate surface with a releasing agent;
h) applying the isolated culturally expanded human marrow-derived mesenchymal cells to a carrier formatted to promote round cell morphology; and,
i) implanting the carrier containing the culturally expanded human marrow-derived mesenchymal cells into the damaged articular cartilage.
13. The method of claim 12, wherein said medium is comprised of BGJ.sub.b Medium with 10% fetal bovine serum.

14. The method of claim 12, wherein said medium is comprised of F-12 Nutrient Mixture.

15. A method for repairing skeletal defects comprising:

a) providing a bone marrow specimen containing human mesenchymal stem cells;

b) adding the bone marrow specimen to a medium thereby producing a bone marrow specimen-medium mixture, wherein said medium contains factors that stimulate mesenchymal stem cell growth without differentiation and allows, when cultured, for selective adherence of only the mesenchymal stem cells to a substrate surface;

c) adding the bone marrow specimen-medium mixture to a density gradient which separates cells into low, medium and high density cell fractions based on differences in density;

d) removing the low density cell fraction from the density gradient;

e) adding the low density cell fraction to the medium used in step (b) to produce a low density cell fraction-medium mixture;

f) culturing the low density cell fraction-medium mixture, thereby selectively adhering only the mesenchymal stem cells to the substrate surface;

g) removing any non-adherent matter from the substrate surface;

h) removing remaining adherent mesenchymal stem cells from the substrate surface with a releasing agent, thereby allowing for the isolated mesenchymal stem cells to be recovered;

i) applying the recovered isolated mesenchymal stem cells to a porous carrier comprised of about 60% hydroxyapatite and about 40% tricalcium phosphate; and,

j) implanting the porous carrier containing the culturally expanded human marrow-derived mesenchymal stem cells into the skeletal defect.

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L8: Entry 13 of 34 File: USPT Nov 3, 1998

DOCUMENT-IDENTIFIER: US 5830708 A
TITLE: Methods for production of a naturally secreted extracellular matrix

DEPR:
The three-dimensional stromal support, the culture system itself, and its maintenance, as well as various uses of the three-dimensional cultures and of the naturally secreted extracellular matrix are described in greater detail in the subsections below. Solely for ease of explanation, the detailed description of the invention is divided into the three sections, (i) growth of the three-dimensional stromal cell culture, (ii) isolation of the naturally secreted human extracellular matrix, and (iii) formulation of the isolated extracellular matrix into preparations for injection at the site of soft tissue defects.

DEPR:
In one embodiment of the present invention, stromal cells which are specialized for the particular tissue to be cultured can be added to the fibroblast stroma for the production of a tissue type specific extracellular matrix. For example, dermal fibroblasts can be used to form the three-dimensional subconfluent stroma for the production of skin-specific extracellular matrix in vitro. Alternatively, stromal cells of hematopoietic tissue including, but not limited to, fibroblast endothelial cells, macrophages/monocytes, adipocytes and reticular cells, can be used to form the three-dimensional subconfluent stroma for the production of a bone marrow-specific extracellular matrix in vitro, see infra. Hematopoietic stromal cells can be readily obtained from the "buffy coat" formed in bone marrow suspensions by centrifugation at low forces, e.g., 3000.times.g. Stromal cells of liver may include fibroblasts, Kupffer cells, and vascular and bile duct endothelial cells. Similarly, glial cells can be used as the stroma to support the proliferation of neurological cells and tissues. Glial cells for this purpose can be obtained by trypsinization or collagenase digestion of embryonic or adult brain. Ponten and Westermark, 1980, In Federof, S. Hertz, L., eds, "Advances in Cellular Neurobiology," Vol. 1, New York, Academic Press, pp. 209-227.

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L11: Entry 12 of 72 File: USPT Jan 11, 2000

US-PAT-NO: 6013853
DOCUMENT-IDENTIFIER: US 6013853 A
TITLE: Continuous release polymeric implant carrier
DATE-ISSUED: January 11, 2000

US-CL-CURRENT: 424/423; 623/11.11, 623/23.75, 623/23.76

APPL-NO: 8/196970
DATE FILED: February 15, 1994

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/123,812 filed Sep. 20, 1993 now U.S. Pat. No. 5,607,474, which is a continuation of Ser. No. 07/837,401 filed Feb. 14, 1992 now abandoned, both of which are fully incorporated herein by reference.

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L11: Entry 18 of 72 File: USPT Mar 2, 1999

US-PAT-NO: 5876452
DOCUMENT-IDENTIFIER: US 5876452 A

TITLE: Biodegradable implant

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
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| Boyan; Barbara D. | San Antonio | TX | N/A | N/A |

US-CL-CURRENT: 623/23.72; 424/424

CLAIMS:

We claim:
1. A porous bioerodible tissue implant device comprising a bioerodible synthetic polymeric material having a uniform non-fibrous composition characterized in that said material has a predetermined uniform porosity and is adapted to be implanted during use into cartilage, said polymeric material having the stiffness and compressibility properties of said cartilage.
2. A molded, porous bioerodible tissue implant device comprising a bioerodible polymeric material, said device having a uniform, substantially solid, composition throughout the volume enclosed by the implant, characterized in that said material has a predetermined uniform porosity and is adapted to be implanted during use into bone, said polymeric material having the stiffness and compressibility properties of said bone.
3. An implant device of claim 1 having access sites for receiving growth of tissue therein comprising passages extending into the material.
4. An implant device of claim 2 having access sites for receiving growth of tissue therein comprising passages extending into the material.
5. An implant device of claim 1 having a growth factor, bioactive agent to induce, promote, or support tissue ingrowth and repair incorporated into said polymeric material.
6. An implant device of claim 2 having a growth factor, bioactive agent to induce, promote, or support tissue ingrowth and repair incorporated into said polymeric material.

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L16: Entry 16 of 60 File: USPT Jan 16, 2001

US-PAT-NO: 6174526
DOCUMENT-IDENTIFIER: US 6174526 B1

TITLE: Blood-borne mesenchymal cells

DATE-ISSUED: January 16, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
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US-CL-CURRENT: 424/93.1; 424/93.7, 435/372, 435/375

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L16: Entry 29 of 60 File: USPT Oct 26, 1999

US-PAT-NO: 5972703
DOCUMENT-IDENTIFIER: US 5972703 A
TITLE: Bone precursor cells: compositions and methods
DATE-ISSUED: October 26, 1999

US-CL-CURRENT: 435/372; 424/139.1, 424/141.1, 424/173.1, 435/325, 435/355, 435/366, 435/378, 530/388.2, 530/388.7, 530/389.6, 530/412, 530/413

APPL-NO: 8/ 289794
DATE FILED: August 12, 1994